

REMARKS**Amendment to the Specification**

The Applicants have amended ¶ 1 of the present specification to delete the priority claim of prior filed U.S. Patent Applications and provide the serial number for a U.S. Patent Application.

The Applicants have amended ¶ 97 of the present specification to delete the embedded hyperlink. The Applicants hereby state that all amendments do not add new subject matter to the specification.

Amendments to the Claims

Claims 1-48 are pending. The Applicants respectfully ask the Examiner to replace all prior versions and listings of claims in the present application with the listing of claims currently provided. Claims 1, 3-6, 10-18, 22, 45-47 were amended, Claims 2, 21, 23-44 were cancelled and Claims 56 and 57 are new. The Applicants hereby state that all amendments do not add new subject matter to the specification.

Support for Claims 1, 3-6, 10-18, 22, 45-47, 56 and 57 can be found throughout the specification, such as, e.g., pg. 8, ¶ 22-23; pg. 10, ¶ 34; pg. 11, ¶ 36; pg. 14, ¶ 52; pg. 15, ¶ 53; pg. 30, ¶ 120; and in U.S. Patent Application Serial No. 10/757,077 (Attorney Docket No. ALLE0014-103, filed January 14, 2004) at pg. 24, ¶ 109; pg. 38, ¶ 156; and pg. 70, ¶ 285, which was incorporated by reference.

Support for Claims 16-20 and 22 can be found throughout the specification, such as, e.g., pg. 5, ¶ 16; and pg. 20, ¶ 76.

Support for Claims 5, 6, 17 and 18 can be found throughout the specification, such as, e.g., pg. 11, ¶¶ 36-40.

Priority

The Examiner has denied the priority claim of the present specification for allegedly lacking to provide adequate support or enablement in the manner provided by 35 U.S.C. § 112, ¶ 1.

According to MPEP § 201.11(III)(G) an applicant may cancel a claim to priority by amending the specification to remove the benefit claim. Thus, the Applicants have amended the specification to cancel the claim to priority.

Claim Objections

The Examiner has objected to Claims 25, 31 and 47 as allegedly encompassing non-elected subject matter. Currently amended Claim 47 encompasses elected subject matter. Claims 25 and 31 were cancelled and, as such, have rendered the objection directed towards these claims as immaterial. Therefore, the Applicants respectfully request withdrawal of the claim objection against Claims 25, 31 and 47.

The Examiner has objected to Claims 17 and 18 as allegedly containing a typographical error of “inclusive.” Currently amended Claims 17 and 18 recite, in part, “inconclusive.” Therefore, the Applicants respectfully submit that Claims 17 and 18 are clear and precise and request withdrawal of the 35 U.S.C. § 112, ¶2 indefinite rejection.

Rejections Pursuant to 35 U.S.C. § 112, ¶ 1 Enablement

The Examiner has rejected Claims 1-48 as allegedly lacking enablement under 35 U.S.C. § 112, ¶ 1. The Applicants respectfully ask for reconsideration under 37 C.F.R. § 1.111.

According to MPEP § 2164.01, the test of enablement is whether a person of ordinary skill in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

BoNT/A substrates

The Examiner contends that the present specification provides enablement for a Clostridial toxin enzymatic activity that results in the cleavage of SNARE proteins. Currently amended Claims 16-20 and 22 are directed towards the processing of a SNAP-25 substrate into enzymatic products by a BoNT/A light chain. Claims 23, 27-30 and 32-44 were cancelled and, as such, have rendered the enablement rejection directed towards these claims as immaterial. Thus, the Applicants submit that the present specification provides adequate enablement for amended Claims 16-20 and 22.

Localization Pattern

The Examiner also contends that the present specification provides enablement support for screening a compound that affects the localization of BoNT/A light chain on the plasma membrane. Currently amended Claims 1, 3-6, 10-18 and 22 are directed towards screening a compound that affects the localization of BoNT/A light chain on the plasma membrane. Claims 33-47 were cancelled and, as such, have rendered the enablement rejection directed towards these claims as immaterial. Thus, the Applicants submit that the present specification provides adequate enablement for amended Claims 1, 3-6, 10-18 and 22.

Conclusion

Therefore, the Applicants submit that the present specification provides adequate enablement for all amended claims and respectfully request withdrawal of the 35 U.S.C. § 112, ¶ 1 enablement rejection against Claims 1-48.

Rejections Pursuant to 35 U.S.C. § 112, ¶ 1 Written Description

The Examiner has rejected Claims 1-48 as allegedly lacking written description under 35 U.S.C. § 112, ¶ 1. The Applicants respectfully ask for reconsideration under 37 C.F.R. § 1.111.

BoNT/A substrates

The Examiner contends that the present specification provides written description support for SNARE proteins that are substrates for Clostridial toxins. Currently amended Claims 16-20 and 22 are directed towards SNAP-25 substrate, a SNARE protein that is a substrate for BoNT/A. Claims 23, 27-30 and 32-44 were cancelled and, as such, have rendered the enablement rejection directed towards these claims as immaterial. Thus, the Applicants submit that the present specification provides adequate written description support for amended Claims 16-20 and 22.

Positive and negative controls

The Examiner also contends that the present specification fails to provide written description support for negative control compounds that have no effects on changing the localization/enzyme activity of a Clostridial toxin light chain or positive control compounds that have effects on changing the localization/enzyme activity of a Clostridial toxin light chain because a particular characteristic of structure of such controls is not indicated.

According to MPEP § 2163.02, the test of written description is whether the specification reasonable conveys to a person of ordinary skill in the art that the applicant was in possession of the claimed invention at the time of filing. Possession may be shown in a variety of ways, including, e.g., by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

First, currently amended Claims 5, 6, 17 and 18 recite a particular characteristic that the each control must have, thereby establishing possession of the claimed invention. Thus, a localization assay negative control compound is a compound known to have no effect on the membrane localization pattern of the BoNT/A light chain in a cell, whereas, a localization assay positive control compound is a compound known to change the membrane localization pattern of the BoNT/A light chain in a cell. Likewise, an enzymatic assay negative control compound is a compound known not to inhibit BoNT/A enzymatic activity, whereas, an enzymatic assay positive control compound is a compound known to inhibit

BoNT/A enzymatic activity. The distinguishing identifying characteristics for each of the controls is sufficient to show that the Applicants were in possession of the claimed invention.

Second, the use of positive and negative controls is well known to a person of ordinary skill in the art. For example, a person skilled in the art would understand that any compound known to have no effect on the membrane localization pattern of the BoNT/A light chain in a cell would be a useful localization assay negative control compound. Furthermore, a person of ordinary skill in the art would understand that such a compound could be, e.g., water, a buffered solution lacking a Clostridial toxin, a Clostridial toxoid or a Clostridial toxin containing an enzymatic inactivating mutation. A person of ordinary skill in the art would know that these same negative controls would also be useful as an enzymatic assay negative control compounds since all these compounds are known not to inhibit Clostridial toxin enzymatic activity.

Likewise, a person of ordinary skill in the art would understand that any compound known to affect the membrane localization pattern of the BoNT/A light chain in a cell would be a useful localization assay positive control compound. Such compounds would include, e.g., Clostridial toxins like BoNT/A. Lastly, a person of ordinary skill in the art would understand that any compound known to inhibit Clostridial toxin enzymatic activity would be a useful enzymatic assay positive control compound. Examples were given on pg. 11, ¶ 40 of the present specification. Thus, the present specification reasonably conveys to a person of ordinary skill in the art that the Applicants had possession claimed subject matter at the time of filing.

Conclusion

Therefore, the Applicants submit that the present specification provides adequate written description support for all amended claims and respectfully request withdrawal of the 35 U.S.C. § 112, ¶ 1 written description rejection against Claims 1-48.

Rejection Pursuant to 35 U.S.C. § 112, ¶ 2 Definiteness***I. The term “alters”***

The Examiner has rejected Claims 1-48 as allegedly being indefinite under 35 U.S.C. § 112, ¶ 2 arguing that these claims fail to particularly point out and distinctly claim the subject matter of the claimed invention. Specifically, the Examiner contends that the term “alters” is unclear. The Applicants respectfully ask for reconsideration under 37 C.F.R. § 1.111.

Amended Claims 1-48 recite, in part, recite “A method of identifying a compound that either reduces or increases a biological persistence of a BoNT/A.” Therefore, the Applicants respectfully submit that Claims 1-48 are clear and precise and request withdrawal of the 35 U.S.C. § 112, ¶ 2 indefinite rejection.

II. The term “less”

The Examiner has rejected Claim 4 as allegedly being indefinite under 35 U.S.C. § 112, ¶ 2 arguing that these claims fail to particularly point out and distinctly claim the subject matter of the claimed invention. Specifically, the Examiner contends that the term “less” is unclear. The Applicants respectfully ask for reconsideration under 37 C.F.R. § 1.111.

Amended Claim 4 does not recite the term “less.” The amendment was made for reasons other than this indefinite rejection and Applicant’s maintain that the term “less” is definite. However, the amendment has made this rejection moot. Therefore, the Applicants respectfully submit that Claim 4 is clear and precise and request withdrawal of the 35 U.S.C. § 112, ¶ 2 indefinite rejection.

III. The term “amount effective to be taken up by the cell”

The Examiner has rejected Claim 11 as allegedly being indefinite under 35 U.S.C. § 112, ¶ 2 arguing that these claims fail to particularly point out and distinctly claim the subject matter of the claimed invention. Specifically, the Examiner contends that the term amount effective to be taken up by the cell” is recited in such a way as to make the term relative, and thus indefinite. The Applicants respectfully ask for reconsideration under 37 C.F.R. § 1.111.

Amended Claim 11 recites, in part, that the amount effective to be taken up by the cell is “the amount able to produce an identifiable membrane localization pattern of the BoNT/A light chain in the cell.” Therefore, the Applicants respectfully submit that Claim 11 is clear and precise and request withdrawal of the 35 U.S.C. § 112, ¶2 indefinite rejection.

IV. The term “GFP-SNAP assay”

The Examiner has rejected Claims 22 and 32 as allegedly being indefinite under 35 U.S.C. § 112, ¶ 2 arguing that these claims fail to particularly point out and distinctly claim the subject matter of the claimed invention. Specifically, the Examiner contends that the term amount effective to be taken up by the cell” is recited in such a way as to make the term relative, and thus indefinite. The Applicants respectfully ask for reconsideration under 37 C.F.R. § 1.111.

The Applicants submit that the term “GFP-SNAP assay” provides a reasonable degree of clarity and particularity defines the claimed invention because the present specification specifically refers to this assay and the patent application that discloses it, see, pg. 29, ¶ 113. Therefore, the Applicants respectfully submit that Claims 22 and 32 are clear and precise and request withdrawal of the 35 U.S.C. § 112, ¶2 indefinite rejection.

IV. The term “enhancement”

The Examiner has rejected Claims 16-22 as allegedly being indefinite under 35 U.S.C. § 112, ¶ 2 arguing that these claims fail to particularly point out and distinctly claim the subject

matter of the claimed invention. Specifically, the Examiner contends that the term "enhancement" is unclear. The Applicants respectfully ask for reconsideration under for reconsideration under 37 C.F.R. § 1.111.

First, the plain meaning of the term "enhancement" is defined as "to increase or improve in quality," see, e.g., Merriam-Webster Online; and *Webster's Third New International Dictionary of the English Language*, unabridged, Merriam-Webster, Inc, (1993). Additionally, the present specification makes clear that "enhancement" when referring to processing of a Clostridial toxin substrate indicates a Clostridial toxin with enhanced enzymatic activity, see, e.g., pg. 19, ¶ 70. Thus, a person of ordinary skill in the art would immediately understand that the phrase "enhancement of processing" of a Clostridial toxin substrate means "to increase or improve the enzymatic activity of a Clostridial toxin."

Second, the present specification discloses many assays that can measure the enhancement of processing of a Clostridial toxin substrate, see, pg. 20, ¶ 70. Thus, a person of ordinary skill in the art would immediately understand how to measure an increased or improved enzymatic activity of a Clostridial toxin based on the assay selection.

The plain meaning of the term "enhancement" provides a reasonable degree of clarity and particularity defines the claimed subject matter to a person of ordinary skill in the art. Therefore, the Applicants respectfully submit that Claims 16-22 are clear and precise and request withdrawal of the 35 U.S.C. § 112, ¶2 indefinite rejection.

Rejection Pursuant to 35 U.S.C. § 101 Obviousness-Type Double Patenting

The Examiner has provisionally rejected Claims 1-48 as allegedly being unpatentable over Claim 60 of U.S. Patent Application 10/732,703, Shengwen Li and Kei Roger Aoki, *Lipid Rafts and Clostridial Toxins* (Dec. 10, 2003) in view of Judit Herreros et al., *Lipid Rafts Act as Specialized Domains for Tetanus Toxin Binding and Internalization into Neurons*, 12 Mol. Biol. Cell 2947-2960 (2001), hereafter the Herreros reference, under the judicially created doctrine of obviousness-type double patenting under 35 U.S.C. § 101. While this provisional

rejection is traversed, the Applicants respectfully defer responding to the rejection until allowable subject matter is indicated.

Rejection Pursuant to 35 U.S.C. § 102(b) Anticipation

The Examiner has rejected Claims 23-32 as allegedly being anticipated under 35 U.S.C. § 102(b) by James J. Schmidt and Karen A. Bostian, *Assay for the Proteolytic Activity of Serotype A from Clostridium botulinum*, U.S. Patent 5,965,699 (Oct. 12, 1999). The Applicants respectfully ask for reconsideration under 37 C.F.R. § 1.111.

Claims 23-32 were cancelled and, as such, have rendered the enablement rejection directed towards these claims as immaterial. Therefore, the Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) anticipation rejection for Claims 23-32.

Rejection Pursuant to 35 U.S.C. § 102(e) Anticipation

The Examiner has rejected Claims 23-32 as allegedly being anticipated under 35 U.S.C. § 102(e) by James J. Schmidt and Robert G. Stafford, *High Throughput Assays for the Proteolytic Activities of Clostridium Neurotoxins*, U.S. Patent 6,762,280 (Jul. 13, 2004). The Applicants respectfully ask for reconsideration under 37 C.F.R. § 1.111.

Claims 23-32 were cancelled and, as such, have rendered the enablement rejection directed towards these claims as immaterial. Therefore, the Applicants respectfully request withdrawal of the 35 U.S.C. § 102(e) anticipation rejection for Claims 23-32.

Rejection Pursuant to 35 U.S.C. § 103(a) Obviousness

I. Obviousness rejections over Schmidt in view of Fernandez-Salas I and Fernandez-Salas II

The Examiner has rejected Claims 1-48 as allegedly being obvious under 35 U.S.C. § 103(a) over James J. Schmidt and Robert G. Stafford, *High Throughput Assays for the*

Fernandez-Salas, E., et al., Methods of Identifying Compounds that Alter Toxin Persistence and/or Protease Activity

Proteolytic Activities of Clostridium Neurotoxins, U.S. Patent 6,762,280 (effective filing date Sep. 25, 2000), hereafter the “Schmidt patent” in view of Ester Fernandez-Salas et al., *Plasma Membrane Localization Signals in the Light Chain of Botulinum Neurotoxin Serotype A*, ABS 9.2 Soc. Neurosci. Abstr. Viewer Itiner. (Nov., 2003), hereafter the “Fernandez-Salas I abstract”; or Ester Fernandez-Salas et al., *Localization of BoNT Light Chains in Neuronal and Non-Neuronal Cell Lines, Implications for the Duration of Action of the Different Serotypes*, 365(Suppl. 2) Naunyn-Schmiedeberg Arch. Pharmacol. ABS R19 (Jun., 2002), hereafter the “Fernandez-Salas II abstract”.

The Examiner contends that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of these references and come up with a method of identifying a compound that alters a biological persistence of a BoNT/A as presently claimed in Claims 1-48. Specifically, the Examiner argues that it would have been obvious to modify the method for identifying a compound that inhibits or enhances the proteolytic activity of BoNT/A disclosed in the Schmidt patent to further measure biological persistence of a BoNT/A because the Fernandez-Salas I abstract and Fernandez-Salas II abstract discloses that BoNT/A light chain co-localizes with SNAP-25. The Applicants respectfully ask for reconsideration under 37 C.F.R. § 1.111.

Schmidt, Fernandez-Salas I and Fernandez-Salas II provide no teaching, suggestion or motivation to combined references.

According to MPEP § 2143.01, obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. The Applicants respectfully submit that a *prima facie* obviousness case fails because the Schmidt patent, the Fernandez-Salas I abstract and Fernandez-Salas II abstract do not provide any motivation, suggestion or teaching that would lead a person skilled in the art to specifically make a method of identifying a compound that alters the biological persistence of BoNT/A comprising the test localization assay and the test enzymatic assay as presently claimed in Claims 1-48.

Pending Claim 1 and the claims depending from this independent claim recite, in part, a method of “identifying a compound that alters a biological persistence of a BoNT/A, the method comprising a test localization assay.” As such, a test compound identified from presently claimed method must exhibit an activity that either shortens the time period that a BoNT/A is active, or lengthens the time period that a BoNT/A is active. The test localization assay does not measure the degree of BoNT/A proteolytic activity that a compound alters at any given time, as does, *e.g.*, the test enzymatic assay recited in pending Claim 16, a dependent claim that further adds the steps of determining BoNT/A proteolytic activity of the test localization assay recited in independent Claim 1

The Schmidt patent discloses an *in vitro* method that for identifying a compound that inhibits or enhances the proteolytic activity of BoNT/A. As such, this reference allegedly discloses the presently claimed method steps of the test enzymatic assay recited in Claim 16. However, the Applicants strenuously disagree with the Examiner’s position that the Schmidt patent only fails to set forth the localization of a BoNT/A light chain to the plasma membrane. The Schmidt patent not only fails to set forth the membrane localization of a BoNT/A light chain, but also fails to identify any sequences responsible for this localization. In addition, the Schmidt patent is utterly silent with respect to any method of identifying a compound that alters a biological persistence of a BoNT/A. In fact, the Schmidt patent is directed to a completely different problem relative to the presently claimed method because it provides a solution for identifying a compound that alters BoNT/A proteolytic activity (*i.e.*, the presence or absence of proteolytic activity at one specific time point), but not one that identifies a compound that alters BoNT/A biological persistence (*i.e.*, the time period that a BoNT/A is proteolytically active). Furthermore, the Schmidt patent teaches *in vitro* proteolytic activity assay and thus is completely deficient in teaching any assay performed in a cell-based system. Thus, the Schmidt patent does not even explicitly or implicitly disclose a cell-based assay useful to identify altered BoNT/A biological persistence, let alone teach, suggest or motivate a person skilled in the art to 1) invent a cell-based assay useful to identify a compound that alters BoNT/A biological persistence; and 2) combine the Schmidt BoNT/A proteolytic activity assay with any kind of assay that measures the duration of

BoNT/A activity over time, *i.e.*, biological persistence, in order to arrive at the presently claimed invention.

The Fernandez-Salas I abstract discloses that BoNT/A light chains localize in the plasma membrane of neurons in the same compartment as SNAP-25. Although this abstract indicates that signals present on the N-terminus and C-terminus of the BoNT/A light chain mediate this localization, there is no guidance with respect to 1) the specific identity of these sequences; 2) the amino acid lengths of these sequences; and 3) whether the N- and C-terminal sequences of the Fernandez-Salas I abstract are the same as or different from the sequences and motifs discussed in the Fernandez-Salas II abstract. The Fernandez-Salas I abstract provides absolutely no information regarding any method useful for identifying a compound that alters a biological persistence of a BoNT/A. In fact, the Fernandez-Salas I abstract is directed at solving the problem of identifying what molecular mechanisms contained within BoNT/A controls its biological persistence and not how to identify a compound that alters the biological persistence of a BoNT/A. At best, the Fernandez-Salas I abstract suggests there is a correlation between the localization of a Clostridial toxin and the duration of biological persistence and that this localization is mediated by undisclosed signals at the N- and C-termini. Thus, the Fernandez-Salas I abstract fails to even explicitly or implicitly teach, suggest or motivate a person skilled in the art to invent a cell-based assay useful to identify altered BoNT/A biological persistence, let alone 1) a cell-based assay useful to identify a compound that alters BoNT/A biological persistence; 2) an *in vitro* BoNT/A proteolytic activity assay useful to identify a compound that alters BoNT/A proteolytic activity; and 3) combine the Schmidt BoNT/A proteolytic activity assay with any kind of assay that measures the duration of BoNT/A activity over time, *i.e.*, biological persistence, in order to arrive at the presently claimed invention.

The Fernandez-Salas II abstract discloses that BoNT/A light chains localize in the plasma membrane of neuronal and non-neuronal cells in the same compartment as SNAP-25. As such, this abstract suffers to an even greater extent than the Fernandez-Salas I abstract because while it mentioned that sequences and motifs important for BoNT/A localization were identified, there was no indication of 1) the identity of these sequences and motifs; and 2) the location where these sequences and motifs were on the light chain. At best, the

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Fernandez-Salas II abstract suggests that there is a correlation between the localization of a Clostridial toxin and the duration of biological persistence and that this localization is mediated by unidentified sequences and motifs somewhere on the light chain. Thus, the Fernandez-Salas II abstract fails to explicitly or implicitly teach, suggest or motivate a person skilled in the art to 1) invent a cell-based assay useful to identify altered BoNT/A biological persistence; 2) invent a cell-based assay useful to identify a compound that alters BoNT/A biological persistence; 3) invent an in vitro BoNT/A proteolytic activity assay useful to identify a compound that alters BoNT/A proteolytic activity; and 4) combine the Schmidt BoNT/A proteolytic activity assay with any kind of assay that measures BoNT/A biological persistence, in order to arrive at the presently claimed invention.

Thus, the Applicants respectfully submit that the assertion of obviousness is unsupported by the cited references because none of these references provide any explicit or implicit teaching, suggestion or motivation to 1) invent a cell-based assay useful to identify altered BoNT/A biological persistence; 2) invent a cell-based assay useful to identify a compound that alters BoNT/A biological persistence; and 3) combine the Schmidt BoNT/A proteolytic activity assay with any kind of assay that measures BoNT/A biological persistence, in order to arrive at the presently claimed invention. As such, it would not have been obvious for a person skilled in the art to modify or combined the BoNT/A proteolytic activity assay disclosed in the Schmidt patent with the Fernandez-Salas I abstract and Fernandez-Salas II abstract, as suggested by the Examiner, in order to arrive at the presently claimed method of identifying a compound that alters a biological persistence of a BoNT/A. Therefore, the Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) obviousness rejection for Claims 1-48.

II. Provisional obviousness rejections over Li in view of Herreros

The Examiner has provisionally rejected Claims 1-48 as allegedly being obvious under 35 U.S.C. § 103(a) over Shengwen Li and Kei Roger Aoki, *Lipid Rafts and Clostridial Toxins*, U.S. Patent Application 10/732,703, (Dec. 10, 2003), hereafter the Li application in view of Judit Herreros et al., *Lipid Rafts Act as Specialized Domains for Tetanus Toxin Binding and*

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Alter Toxin Persistence and/or Protease Activity

Internalization into Neurons, 12 Mol. Biol. Cell 2947-2960 (2001), hereafter the Herreros reference.

According to MPEP 706.02(k), a provisional obviousness rejection under 35 U.S.C. § 103(a) can be overcome by a showing that the subject matter of the prior art application and the presently claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

The Applicants submit that both the present patent application and the Li application were subject to an obligation of assignment to the same person at the time the presently claimed invention was made. Allergan, Inc is the assignee of both the present patent application and the Li application. All inventors from both the present patent application and the Li application were employees of Allergan, Inc. under an expressed obligation to assign all inventions to Allergan, Inc. The inventions disclosed in both the present patent application and the Li application were invented by the inventors at the time that all the inventors were employees of Allergan, Inc.

Thus, the Applicants respectfully submit that a *prima facie* case of obviousness cannot be made because the subject matter of the Li application is disqualified as 35 U.S.C. § 103 prior art because the subject matter of both applications were under an obligation of assignment to the same person at the time the presently claimed invention was made. Therefore, the Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) obviousness rejection for Claims 1-48.

CONCLUSION

For the above reasons the Applicants respectfully submit that the claims are in condition for allowance, and the Applicants respectfully urge the Examiner to issue a Notice to that effect. Should there be any questions, the Examiner is invited to call the undersigned agent. Please use Deposit Account 01-0885 for the payment of any extension of time fees under 37 C.F.R. § 1.136 or any other fees due in connection with the current response.

Respectfully submitted,

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